Ensuring Quality Pharmacy
Compounding: Implications for Pharmaceutics Education

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Objectives

- Role of the USP in ensuring best practices in pharmacy compounding
- Current USP standards regarding compounding personnel and training
- Future initiatives of USP with regard to ensuring best practices in pharmacy compounding (emphasis on personnel and training)
- Expectations for pharmacy education with regard to ensuring best practices in pharmacy compounding
Outline

I. Introduction
II. US Pharmacopeia
III. USP Chapters <795>, <797> and <1163>
IV. Pharmacy Compounding Regulations
V. Future initiatives
VI. Expectations for pharmacy education
Role of the Compounding Pharmacist

“Individualizing Drug Therapy”
I. Introduction

- History of Pharmaceutical Compounding
- Reasons for Growth
- Special Patient Populations
History of Pharmacy

Compounding in the U.S.

- In the past, *Compounding Was Pharmacy*
- 1900s gave way to commercially prepared pharmaceuticals
- Many strengths/dosage forms available
- Economics changed all that
- Limited strengths/dosage forms
- “One Size Fits All” approach
Reasons for the Growth of Pharmacy Compounding

- Limited dosage forms
- Limited strengths
- Home health care
- Hospice
- Nonavailable drug products/combinations
  - Discontinued Drugs
  - Drug Shortages
- Orphan drugs
- Veterinary compounding
- New therapeutic approaches
- Special Patient Populations
SPECIAL PATIENT POPULATIONS

- Pediatrics
- Geriatrics
- Bioidentical Hormone Replacement Therapy
- Pain Management
- Dental Patients
- Environmentally & Cosmetic Sensitive
- Sports Injuries
- Veterinary Compounding
  - Small, Large, Herd, Exotic, Companion
II. U.S. PHARMACOPEIA

Setting Official Standards for Drugs in the U.S. since 1906
Pharmacopoeias of the U.S.

- Jan 1820: First U.S. Pharmacopeial Convention
- Dec 1820: First U.S. Pharmacopeia was published
  - 272 pages containing 217 drugs/preparations
Pharmacists Pharmacopeia

- 1820  USP developed for pharmacy
- 1900’s  USP became more oriented towards manufacturing
- 2000’s  USP must meet the needs of both pharmacists and manufacturers
Almost 200 official monographs related to compounding

More monographs being prepared

4 official chapters
- USP <795> Pharmaceutical Compounding-Nonsterile
- USP <797> Pharmaceutical Compounding-Sterile
- USP <1163> Quality Assurance in Pharmaceutical Compounding
- USP <1160> Pharmaceutical Calculations

Stability Studies
Uniform Formulations

- Official monographs
- Documented beyond-use dates
- Patient receives same preparation all over the U.S.
III. USP Chapters <795>, <797>, and <1163>

- **USP <795>**
  - Pharmaceutical Compounding-Nonsterile Preparations

- **USP <797>**
  - Pharmaceutical Compounding-Sterile Preparations

- **USP <1163>**
  - Quality Assurance in Compounding
Three Categories-Nonsterile

I. Simple
II. Moderate
III. Complex
Three Categories-Sterile

I. Low-Risk
II. Moderate-Risk
III. High-Risk
USP Chapter <795>, Revised

Pharmaceutical Compounding: Nonsterile Preparations
USP <795> Outline
Revised 2009

- Introduction
- Definitions
- Categories of Compounding
- Responsibilities of the Compounder
- Compounding Process
- Compounding Facilities
- Compounding Equipment
- Component Selection, Handling, and Storage
USP <795> Outline (Cont’d)

- Stability Criteria and Beyond-Use Dating
- Packaging and Drug Preparation Containers
- Compounding Documentation
- Quality Control
- Patient Counseling
- Training
- Compounding for Animal Patients
USP Chapter <797>

Pharmaceutical Compounding-
Sterile Preparations
Introduction
Organization of this Chapter
Definitions
Responsibility of Compounding Personnel
CSP Microbial Contamination Risk Levels
Personnel Training and Evaluation in Aseptic Manipulation Skills
Immediate-Use CSPs
USP <797> Content

- Single-Dose and Multiple-Dose Containers
- Hazardous Drugs as CSPs
- Radiopharmaceuticals as CSPs
- Allergen Extracts as CSPs
- Verification of Compounding Accuracy and Sterility
- Environmental Quality and Control
- Suggested Standard Operating Procedures (SOPs)
USP <797> Content

- Elements of Quality Control
- Verification of Automated Compounding Devices for Parenteral Nutrition Compounding
- Finished Preparation Release Checks and Tests
- Storage and Beyond-Use Dating
- Maintaining Sterility, Purity, and Stability of Dispensed and Distributed CSPs
USP <797> Content

- Patient or Caregiver Training
- Patient Monitoring and Adverse Events Reporting
- Quality Assurance Program
- Appendices
IV. Pharmacy Compounding Regulations

- Pharmacy State Boards
- Food & Drug Administration
- Drug Enforcement Agency
- OSHA-EPA
State Boards of Pharmacy

- Regulating the practice of pharmacy
- Some states are very active
- Other states are not very active
- National Association of Boards of Pharmacy
FDA ACTIVITIES

- **1938** Compounding regulated by states
- **1938** FDA Created for manufacturers
- **1938** FDA regulated manufacturers
- **1938** State Boards regulated compounding

Mid 1990s FDA began investigating a number of pharmacies that were compounding large quantities of selected drug products.

Manufacturing under the guise of compounding

FDA is trying to bring compounding under their jurisdiction by their definition of “New Drugs”
FDA considered compounded preparations as “New Drugs” and subject to the New Drug Provisions
– IND
– NDA
– Safety
– Efficacy

Enforcement Activities
New Drug Issue

- Compounding DOES NOT create “New Drugs” as defined by the FDA.

- Square pegs don’t fit into round holes!

- Let’s look at the following....
1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof.
“Labeling”

...includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.
“Labeling”

...means any display or written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.

CFR 21 Ch 1 (4-1-08 Edition); 1.3 Definitions
Compounding is a part of the professional practice of pharmacy.

The practice of pharmacy is governed by the state boards of pharmacy.

The state boards of pharmacy have authority over labels for dispensing prescriptions, including compounded prescriptions, in their states.
V. Future Initiatives

- Expand Accreditation (PCAB)
- Monograph Development (USP)
- Introduce Certification
- Expanded Quality Assurance Activities
- Expand Educational Offerings
Quality Issues

- Standards for Quality
- Standard Operating Procedures
- Testing (Analytical, Microbiological)
- Beyond Use Dating
Standards for Quality

- cGMPs
- cGCPs
- CPGs
- USP
- FDA
Written procedures should exist for all compounding, quality control, packaging and labeling processes.

Master Formula Records should be written to provide adequate instruction and documentation of the compounding operation.
Testing

- Physical observation
- Potency, Analytical
- Sterility
- Endotoxin
- Other
ANALYTICAL METHODS**

- Weight*
- Volume*
- Macro/Micro*
- pH*
- Osmolality*
- Refractive Index*
- Specific Gravity*

- Melting Point*
- UV/Vis/IR Spectroscopy
- HPLC
- GC
- Sterility*
- Endotoxin*
VI. Compounded Dosage

Forms
Traditional Compounded Dosage Forms

Oral Solids (Capsules, Tablets)
Oral Liquids (Solutions, Susp, Emulsions)
Topicals (Creams, Ointments, Gels)
Suppositories, Inserts
Injectables
Troches/Lozenges
Nuclear Pharmaceuticals
Intravenous Admixtures
Many, many others....
Newer Dosage Forms

- Rapid-Dissolving Tablets
- Gummy Gels
- Oral Pastes (VET)
- Lollipops
- Mini Lollipops
- Popsicles
- Minitroches
- Sublingual drops

- Transdermal PLO Gels
- Rapid-Penetrating Topical Solutions
- Intrathecal Pain Management
- Sponge Disks
- Implantable Beads
- Iontophoresis/Phonophoresis
Newest Dosage Forms

- Liposomes for Nail Delivery
- Films
  - Skin
  - Topical
- Pluronic Gels
  - Chest cavity
  - Esophageal
- Nasal Spray-Gels
- Gel-Creams
VII Expectations for Pharmacy Education
Educational Needs

- Dosage Forms/Formulation
- Physical Pharmacy
- Drug Stability
- Analytical Methods
- Microbiological Methods
- Calculations
- Experiential Rotations
- Compounding Laboratories
Extent of Pharmacy Compounding

- NCPA: 76% of Membership
- Hospitals: Almost 100% compound
- Chains: About 10% of stores compound
- Total % Rxs: Estimated about 10% of all
- % RPh: Estimated about 25% do some compounding in their practice
Summary

- Patient care often involves specialized medications
- Specialized medications require compounding
- Compounding pharmacists are some of the most involved clinical pharmacists in practice today (worldwide)
- Pharmacists should be the best trained to do this… but are we?